

R E M A R K S**Status of the claims**

Claims 1-6, 10-16 and 27-30 are pending in the application. Claims 1-6 and 10-16 are withdrawn and claims 7-9 and 17-26 are cancelled. New claims 27-30 are presented herein. New claims 27-30 correspond to cancelled claims 19-26, except being presented in proper format for US patent practice. No new matter has been added by these claims. As such entry and consideration thereof are respectfully requested.

Rejections under 35 USC §§ 101 and 112, 2nd paragraph

Claims 19-26 have been rejected under 35 USC §§101 and 112, 2nd paragraph as being improperly drawn to non-statutory “uses”. Claims 19-26 have been cancelled and replaced with new claims 27-30, which are properly directed to “methods of use” and particularly point out and distinctly claim the subject matter, which the Applicant regards as the invention, in this case, methods for recovering endocrine pancreatic function in a patient.

Rejections under 35 USC § 103(a)

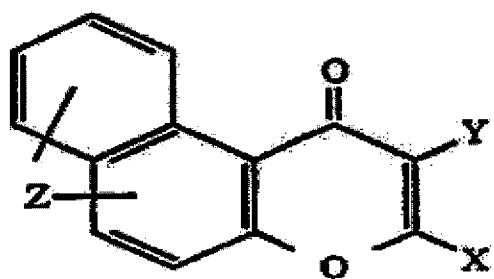
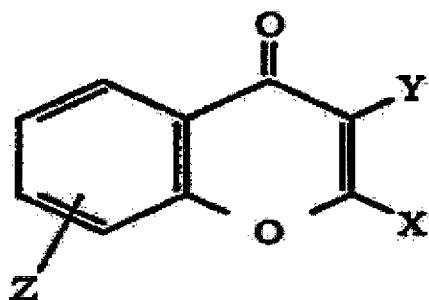
Claims 19-26 have been rejected under 35 U.S.C. §103 as being obvious over Bibbs et al. (US ‘128), in view of Soto et al. and Coote et al. (US ‘034). Bibbs et al. is asserted to teach methods of treating high blood glucose or high blood cholesterol with “a composition comprising less than 40% of other naturally occurring bioflavanoids”. Soto et al. is relied upon for teaching that silymarin is protective against the oxidative peroxidation of cells and activity as a free radical scavenger. The Examiner asserts that evidence shows that diabetes mellitus and its sequels are conditions, which involve free radicals. Coote et al. is generally relied upon for teaching a process of preparing emulsions and compositions. The Examiner asserts that it would have been obvious to one of ordinary skill in the art to combine the teachings of Bibbs et al., Soto et al. and Coote et al. to achieve the instant invention. Applicants traverse this rejection and withdrawal thereof is respectfully requested.

The prior art references do not, in combination, disclose or suggest a method of recovering endocrine pancreatic function with the oral administration of a composition

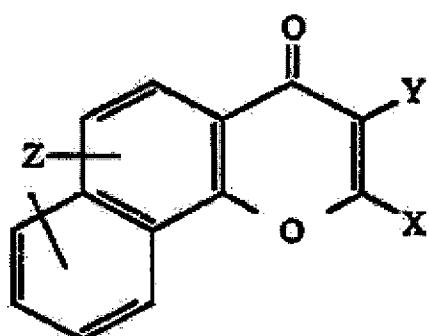
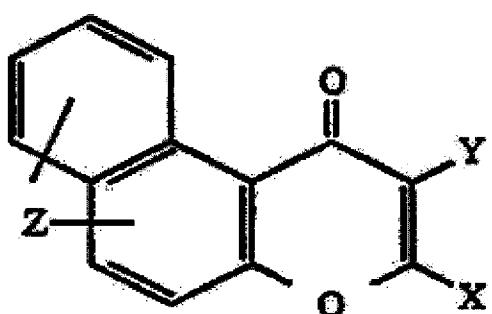
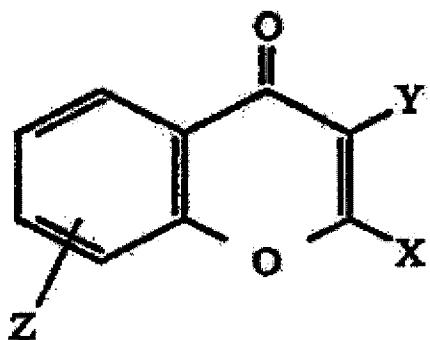
comprising silymarin and carbopol. Bibbs et al discloses in paragraph [0013] an anti-diabetic activity (without indicating what type of diabetes is being treated) of the flavanoid **isovitexin**. Bibbs et al. further describes that other bioflavanoids (without indicating which) having certain chemical structural similarities also exhibit blood-glucose content lowering properties. Bibbs et al. discloses in paragraph [0014] the treatment of a mammal having a high blood glucose with a composition “comprising an effective amount of isovitexin or a pharmaceutically acceptable salt, ester, amide or prodrug thereof, where the composition comprises less than 50% of other naturally occurring bioflavanoids.” (*emphasis added*) The Examiner is clearly misconstruing the teachings of Bibbs et al. The recitation in Bibbs et al. “where the composition comprises less than 50% of other naturally occurring bioflavanoids” is standard language indicating that the active component in the composition of Bibbs et al. is the isovitexin (or analogs, prodrugs etc. of isovitexin) and other bioflavanoids are to be avoided.

Bibbs et al. teaches that isovitexin or a derivative of the same can lower of blood glucose content in an organism. Bibbs et al. disclose in paragraphs [0042] through [0046] the mechanism of action of isovitexin in reducing the glucose concentration in the organism. There is simply no mention or reference whatsoever made in Bibbs et al. of the using of silymarin and carbopol. The only mention of carbopol in Bibbs et al. is a passing reference in a laundry list in [0064] that a dragee core may optionally contain “gum arabic, talc, polyvinyl pyrrolidone, carbopol gel, polyethylene glycol and/or titanium dioxide, lacquer solutions, and suitable organic solvents or solvent mixtures”. There is no suggestion in Bibbs et al. of selectively choosing carbopol to be used in a composition.

As noted by the Examiner, silymarin is a bioflavanoid. However, there is no suggestion, nor motivation, to one skilled in the art to selectively replace isovitexin with silymarin. Despite the fact that silymarin is a bioflavanoid, its choice as a regenerator of endocrine pancreatic function is not obvious due to the great variety of existing bioflavanoids found in nature and their diversity in chemical structure. For example, the following structure is for an isovitexin extracted from barley.



The following show alternative structures for bioflavanoids



The above-mentioned chemical structures are known generally as (or have the generic name of) bioflavanoids but have very different chemical structures, as well as very different biological activity.

Soto et al. discloses the effect of silymarin as an antioxidant and that the reduction of blood glucose observed is due to the capture of free radicals by which cell damage of pancreatic tissue was prevented. Soto et al. thus highlights the protective effect of silymarin in diabetes mellitus. However, the experimentation in Soto et al. did not consider a regenerative effect. In addition, the instant invention is directed to a composition containing a combination silymarin and carbopol. There is no suggestion in Soto et al. of such a combination. Nor is there any disclosure or suggestion in Soto et al. regarding any regenerative activity. While Soto et al. is used prophylactically to prevent the damage that could result from alloxane, the subject matter of the instant claims is directed to the curative activity with damaged pancreatic cells.

The Examiner relies on tenuous conjecture on pages 6 and 7 of the Office Action to form the basis of the rejection.

- 1) For example, on page 6 the Examiner states that it is hypothesized (i.e. not actually known) that free radicals may be involved in diabetes mellitus.
- 2) On page 7, the Examiner notes that Soto et al. “suggests” a protective effect of silymarin against the action of alloxan.
- 3) The Examiner then relies upon this suggested finding to further “suggest” that this proposed action “may” be why silymarin has a protective effect on pancreatic lipid peroxidation.
- 4) Another leap is then made to note that this possible, but not actually shown, mechanism of action on pancreatic lipid peroxidation, “may” contribute to the regulation of plasma glucose.
- 5) The Examiner then notes that it has been “suggested” that thiol groups are important in the intracellular and membrane redox state of the secretory function of beta pancreatic cells. The Examiner relies on this suggestion to propose that silymarin induces an increase in pancreatic glutathione which “may” induce a GSH/GSSG ratio and thereby improve plasma glucose regulation.

Thus, the Examiner relies on at least five separate conjectures or hypotheses from Soto et al. to conclude that one skilled in the art would have been motivated to selectively replace the isovetexin in Bibbs et al. with the silymarin from Soto et al. for the purposes of regenerating damaged pancreatic cells, an activity which is not even considered in Soto et al. One skilled in the art would not be motivated to achieve the instant invention based on the combined teachings of Bibbs et al. and Soto et al. Nor does Cootes et al. provide the motivation and teachings lacking from Bibbs et al. and Soto et al.

Coote et al. discloses a process of preparing an emulsion of natural substances, such as flavanoids, phytosterols and carotenoids. In Coote et al., the combination of the emulsions with carbopol is disclosed only for purposes of forming a paste and its function is as a thickener. In addition, nowhere in Coote et al. is there any teaching or suggestion of having the specific combination with silymarin. Thus, despite the fact that Coote et al. discloses carbopol as an excipient, there is simply no teaching or suggestion of using it specifically with silymarin or using it in a method for regenerating the endocrine pancreatic function.

Thus, it can be concluded that the prior art references cited by the Examiner neither teach, anticipate or suggest individually or in combination the subject matter of the instant claims. As such, withdrawal of the rejection and allowance of the claims are respectfully requested.

In view of the above amendments and Remarks, Applicant believes the pending application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact MaryAnne Armstrong, Ph.D., Reg. No. 40,069 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for

Dated: December 18, 2007

Respectfully submitted,

By 
Mary Anne Armstrong, Ph.D.
Registration No.: 40,069
BIRCH, STEWART, KOLASCH & BIRCH, LLP
8110 Gatehouse Road
Suite 100 East
P.O. Box 747
Falls Church, Virginia 22040-0747
(703) 205-8000
Attorney for Applicant